PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BLOcp644/83P	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/IB 03/05108	International filing date *(day/month/year)* 16.10.2003	Priority date *(day/month/year)* 16.10.2002
International Patent Classification (IPC) or national classification and IPC C07K7/08		
Applicant CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 12 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.05.2004	09.12.2004
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International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-34 as originally filed

   Claims, Numbers

   1-23 as originally filed

   Drawings, Sheets

   1/12-12/12 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,2,8,9-15,20-23 (all partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1,2,8,9-15,20-23 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☒ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-4, 6, 8-17, 19-23 (partially); 5 and 18 (completely) (inventions 1 and 18) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely)
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely)
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The applicant has paid examination fees only for inventions 1 and 18. Therefore, this report does not relate to inventions 2-17,19-26 for which examination fees have not been paid.

2. Furthermore, this IPEA will not give an opinion for the subject-matter of claims 1, 2, 8, 9-15, 20-23 for which an ISR was not established (Rule 66.1(e) PCT). This IPEA agrees with the objections raised by the ISA justifying the partial search report (see ISA and points 12-13, below).

3. Thus, this report would not give an opinion for the subject-matter of claims 1-4, 6, 8,-17, 19-23 (all partially); 7, 8 (completely).

Re Item IV

Lack of unity of invention

4. The present application lacks unity (Rule 13 PCT). The following inventions have been found:

Invention 1. Claims 1-4, 8-17; 20-23 (all partially); 5 and 18 (all completely): Peptide of SEQ. ID. No: 1, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 2. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No.: 2, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 3. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 3, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 4. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 4, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 5. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 5, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 6. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 6, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 7. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 7, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 8. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 8, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 9. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 9, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 10. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 10, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 11. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 11, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 12. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 12, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 13. Claims 1-4, 9-17, 20-23 (all partially); 7 and 8 (all completely): Peptide of SEQ. ID. No: 13, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 14. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 14, uses

and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 15. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 15, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 16. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 16, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 17. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 17, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 18. Claims 1-4, 6, 9-17, 19-23 (all partially): Peptide of SEQ. ID. No: 18, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 19. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 19, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 20. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 20, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 21. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 21, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 22. Claims 1-4, 6, 9-17, 19-23 (all partially): Peptide of SEQ. ID. No: 22, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 23. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 23, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and

host cells.

Invention 24. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 24, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 25. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 25, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

Invention 26. Claims 1-4, 9-17, 20-23 (all partially): Peptide of SEQ. ID. No: 26, uses and compositions thereof, polynucleotide encoding the same, recombinant vector and host cells.

The peptides of the present application would be regarded as having the same or corresponding technical feature (Rule 13.2 PCT) if the alternatives had a common property or activity, and either shared a significant structural element which constitutes a structurally distinctive portion over the prior art or belong to a recognized class of chemical compounds expected to behave in the same way (Administrative instruction of the PCT, Annex B, Part 1, paragraph (f).

The fact that all the peptides have a common property is not sufficient to establish unity of invention because the SEQ. 1-26, which impart the common property, do not share a significant structural which constitutes a structurally distinctive portion over the prior art art nor belong to a recognized class of chemical compounds expected to behave in the same way. Thus, PSA mimetic peptides are already known in the art from (D1) Shin et al. (2001) Infection and immunity 69, 3335-3342; (D2) Hurpin et al. (1992) Hybridoma 11, 677-687 and (D3) WO-A-9808874, and it is not expected that all the peptides consisting of 5-30 amino acids have the present property or activity.

The antibodies of D1 (Table 2, HmenB1), D2 (Table 1 SEAM-12, SEAM-18 and SEAM-28) and D3 (30H12) specifically react with PSA attached to NCAM, since said antibodies react with CHP-134 cells (in the case of D1; Table 2 and D2; Table 1) or are known anti-PSA-NCAM antibodies (in the case of D3).

The peptides identified using those antibodies comprise a B epitope of PSA attached to NCAM, which is recognized by an anti-PSA antibody (see the peptides of D1, Table4,

first and second peptides; D2, Table 4, pep 1, pep 4, pep 5, pep 6, pep 7, pep 8, pep 12 and pep 67).

Thus, a division into the aforementioned inventions should be made as the present peptides are considered as alternative PSA mimetopes to those of the prior art that do not meet the requirements of Administrative instruction of the PCT, Annex B, Part 1, paragraph (f).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5. Reference is made to the following documents:

D1: SHIN J S ET AL: "Monoclonal Antibodies Specific for Neisseria meningitidis Group B Polylsaccharide and Their Peptide Mimotopes" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 69, no. 5, May 2001 (2001-05), pages 3335-3342, XP002228383 ISSN: 0019-9567

D2: WO 98/08874 A

D3: HURPIN C M ET AL: "BACTERICIDAL ACTIVITY OF TWO IGG2A MURINE MONOCLONAL ANTIBODIES WITH DISTINCT FINE SPECIFICITIES FOR GROUP B NEISSERIA MEINGITIDIS CAPSULAR POLYSACCHARIDE" HYBRIDOMA, LIEBERT, NEW YORK, NY, US, vol. 11, no. 6, 1992, pages 677-687, XP009004404 ISSN: 0272-457X

D4: WO 02/46408 A

D5: WO 00/54805 A

6. **This reports relates exclusively to inventions 1 and 18, which encompass the peptides of SEQ. ID. Nos.: 1 and 18.**

Claims 1-4, 8-17, 20-23 (partially); 5 and 18 (completely) belong to invention 1.

Claims 1-4, 6, 9-17, 19-23 (partially) belong to invention 18.

7. Novelty (Art. 33 (2) PCT.

(D1) discloses peptides obtained after screening two 7-mer libraries with Ab obtained after immunization with alpha(2,8)-polysialic acid from E. Coli K1. The Ab735 used in the examples of the application is also an Ab against alpha(2,8)-polysialic acid from E. Coli K1.

(D2) discloses the preparation of B epitopes by screening a phage library with mAbs against PS.

(D3) discloses anti-idiotypic monoclonal antibodies against 30H12, a mAb against alpha(2,8) polysialic acid obtained after immunization with live group B meningococci. The anti-idiotypic mAb mimics alpha (2,8) polysialic acid.

(D4) discloses the activities of the interaction PSA-NCAM, which include those disclosed in the application.

(D5) Seq. 3 is the same as seq. 13 of the application. However, this documents relates to a different problem.

The prior art does not disclose the peptides of SEQ. ID. Nos: 1 and 18. Therefore, the subject-matter of claims 1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely) is novel.

8. Inventive step (Art. 33 (3) PCT.

The present peptides of SEQ. ID. Nos: 1 and 18 are neither disclosed nor suggested in the prior art, let alone their use in modulating NCAM functions. Therefore, the subject-matter of claims 1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely) is considered to be inventive.

9. Industrial applicability (Art. 33(4) PCT).

The subject-matter of claims 1-4, 6, 8-17, 19-23 (all partially) and 5, 18 (all completely) meets the provisions of Art. 33(4) PCT.

Re Item VII

Certain defects in the international application

10. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D2-D5 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

11. Claims. 12-13 are unclear, since they relate to a medicament or composition comprising the peptide or peptide complex of claims 1-7 or 9. However, claims 1-7 or 9 do not relate to peptides or peptide complexes but to use claims.

12. Independent claims 1 and 14 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, namely peptides that bind to anti-PSA antibodies and modulate NCAM, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result (chemical formula of said peptides). This information is also not found in claims 2, 8, 9-13, 15 and 20-23, which share the same defects as claims 1 and 14.

13. Independent claims 1 and 14 do not meet the requirements of Arts 6 PCT. The subject-matter of claims 1 and 14 is not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and the functional features do not allow the scope of the claim to be ascertained (PCT Guidelines 5.35). Claims 1 and 14 relate to peptides comprising B epitopes of a PSA attached to NCAM and that modulate NCAM functions. The description is silent with regard to the structure needed by the peptides to bind to anti-PSA attached to NCAM antibodies and modulate NCAM functions. Only few examples of peptides binding to anti-PSA antibodies are given in the description (SEQ. ID. No.: 1-26). Only three of them, SEQ. ID. No: 1, 18 and 21, are shown to modulate NCAM functions. Therefore, present claims 1 and 14 are not supported in their whole breadth. On the other hand, the fact that any peptide could be screened does not overcome this objection, as the skilled person would not have knowledged beforehand, except for the peptides of SEQ. ID. No.: 1, 18 and 26, as to whether it would fall within the scope claimed. Undue experimentation would be required to randomly screen peptides that bind to anti-PSA (attached to NCAM) antibodies and that modulate NCAM functions. Claims 2, 8, 9-13, 15 and 20-23 share the same defects as claims 1 and 14.